

Updated: 12/24/08

Dercum's disease or adiposis dolorosa (AD) is thought to be a rare disorder whose hallmark is multiple fatty growths¹ which I will call lipomatosis as the growths tend to be multiple and can be spread over large areas. The lipomatosis is generally as unencapsulated lipomas, fibrolipomas or angioliipomas. In AD and FML with lipoma dolorosa and lipedema, the lipomatosis is painful to touch likely because of an exposure of the nerves in the fat to cytotoxins such as free fatty acids (one of the most toxic substances in the body), cytokines and other cell mediators. The fascia appears to be increased in and around the lipomatosis of AD perhaps participating in the stimulation and growth of the adipose (fat) cells within the lipomas. Inflammatory cells including lymphocytes, macrophages and eosinophils secrete factors causing necrosis and damage of tissue resulting in pain, and participate in the growth process by secreting growth factors; the actual stimulus for the fascia or adipose tissue growth is not known. These changes in the AD tissue suggest not only a problem with the immune system but an over-activation of damaging enzymes in the tissue. There are no proven treatments for AD to date. In this monograph, you will find recommendations that may or may not help you. Until proven, these recommendations are for you and your doctor to think about and make choices based on your disease, medical history and overall current situation.

I recommend the following for the treatment of AD:

Recommendation I: Diet

We have no idea at this time what causes the lipomatosis – is it metabolic, meaning that there is some pathway that is some metabolic pathway that is altered in AD? Is it genetic? Autoimmune? Infectious? We do know fat is increased. We also know that fat is a repository for (lipophilic) toxins² and that fat loss improves their excretion from the body. Our goal is therefore to improve fat loss in a healthful manner.

- With this in mind, I recommend avoidance of all hydrogenated oils, period. No margarine. No packaged food with hydrogenated oils. You can substitute olive oil or other natural oils instead. According to Caroline Pond³⁻⁶, increasing omega-3-fatty acids in the diet inhibits the growth of fat around infected lymph nodes, so choosing an oil with high omega-3 fatty acids would be best especially for those of you with hyperplastic (enlarged but “normal” lymph nodes with increased fat content). The oils high in omega-3-fatty acids include flax, olive, cod liver or amaranth oil. Oral cod liver oil intake has been demonstrated to decrease (but not eliminate) NSAID use in those with arthritis⁷.
- I would also recommend the addition of the amino acid glycine and arginine to your diet (see below).
- Eat whole raw grains. Grains are seeds and can help decrease growth of fat tissue (see below under protease inhibitors).
- Avoid red meats. Although I am a vegetarian, I recommend you choose a healthy diet containing the foods you like. However, there has been some intriguing research on sialic acids that lead me to recommend that you eliminate red meat from your diet (beef and lamb), pork and limit turkey. Sialic acids are typically found as the end carbohydrates (monosaccharides) attached to glucose type molecules (glycoconjugates) on cell surfaces. They play many important roles in many physiological and pathological processes, including microbe binding that leads to infections, regulation of the immune response, the progression and spread of human malignancies, etc. Some sialic acid residues in our bodies are different from those in beef, lamb, pork and turkey (as well as non-human primates, etc)⁸. If you eat these meats, your body recognizes the

sialic acid residues biochemically as normal and incorporates them into the daily workings of cells. However your immune system recognizes them as abnormal and mounts an immune response or an inflammatory response which includes the production of antibodies. If you have other autoimmune disorders or are experiencing inflammation, my recommendation would be to limit your meat ingestion to fish and chicken with turkey only on Thanksgiving (in the USA). In fact, I know a few people with FML and lipoma dolorosa that go into a flare if they eat red meat.

- Avoid dairy products as they too contain the “different” sialic acid residue that then induces an antibody response in our bodies. If you have to have dairy products, try and avoid non-organic dairy products that may contain pesticides, growth hormone and antibiotics.
- Get a good multivitamin; one that has vitamins and minerals that can be absorbed. Here are some good ones:

- <http://www.integratedhealth.com/hpdspec/two.html>
- http://www.beyondhealth.com/Multi_Vit-Min_Formula.aspx

You can read more about the best ingredients that can be easily absorbed at www.beyondhealth.com.

- One hypothesis for the lipomatosis is that they accumulate fat that is not as reusable as other areas of fat. In addition, as fat increases, unoxidized long chain fatty acids can enter toxic pathways in non-adipose tissues⁹. I suggest the following as a 6-month trial (100 days at a minimum):
 - a. Use medium chain oil (MCT oil) for cooking, salad dressing, or in anything requiring oil to decrease the intake of long or very long chain fatty acids. Limit oil intake to less than 80 grams at a time (over five tablespoons) to avoid intense intestinal cramping. MCT oil can be obtained from health food stores and can cost as little as \$7.50 for 16 fl oz. Both Novartis and Mead Johnson make MCT oil as well.
 - b. Use Portagen®, a Milk-based powder with 87% of fat from medium-chain triglycerides (MCT) with corn oil to provide the essential linoleic acid as a substitute for milk when cooking (or when drinking milk products) whenever possible. Portagen® is often prescribed for children. More information can be found at: http://www.intekom.com/pharm/bm_squib/portagen.html. A one pound can costs about \$22 and may be cheaper by the case.
 - c. If Portagen® use is low, so that linoleic consumption is lower, replenish Omega 3 fatty acids once weekly with Lovaza by prescription or over-the-counter fish oil supplements; and
 - d. Take a daily MVI for trace minerals.

MCT oil depresses weight gain and decreased adipose deposits in rats¹⁰, overweight men¹¹ and in healthy men and women where it also increased fat oxidation¹². This diet is best done with the help of a nutritionist, especially if you are on lipid lowering medication and with the knowledge that we are braving new ground. There is one report that suggests that dietary restriction of long-chain triglycerides provides some relief of edema in these patients¹³.

If you are feeling well on your MMP inhibitors (see below) but still feel worn out by exercise or your muscles just don't work like they should, it may be that your energy making machinery (tricarboxylic acid cycle) is depleted making glycogen breakdown and usage difficult. Consider adding **triheptanoin oil** (a 7 carbon fatty acid) found in coconut oil (you may be able to purchase this as pure oil at www.sasolos.com/products/pdf/Excipients_Pharmaceuticals.pdf). Adding triheptanoin to your diet to improve the TCA cycle is called an **anaplerotic diet**.

Recommendation II: Exercise.

Many individuals with fat disorders can exercise and do well with non-impact exercise such as walking, warm pool therapy, gentle stretching. The goal is to not traumatize your tissue as this will increase enzymes in the tissues (**MMPs and other proteases – see below**) important in fat growth. You can lift weights that do not put undue stress on your tendons and muscles – start at a low weight, low repetitions and increase slowly as tolerated. Heat your body prior to exercise to improve your flexibility. Exercise in a warm not a cold environment. Consider relaxation therapy prior to starting exercise for the day. Exercising also makes you sweat which is one way to excrete toxins from your body. Drinking plenty of fluid as you exercise and stimulate fat breakdown will also help in excretion of toxins through the liver (bile) and the kidney. If you can sauna as part of your exercise program to help you sweat out additional toxins, do so. If you find that you cannot tolerate your current exercise, Jacuzzi, sauna program, work with a physiatrist or other to design a program that works for you. Try and start an exercise program after you have started on MMP inhibitors and N-acetyl cysteine to decrease exercise-induced flare. Add triheptanoin to your diet if needed (see above).

Recommendation III: Enzyme inhibitors

Matrix metalloproteinases (MMPs) were characterized initially by their extensive ability to degrade extracellular matrix proteins. Some of the MMPs are involved in normal cell apoptosis and some are triggered by pathological processes like inflammation, ischemia, necrosis, tumor invasiveness, etc. Tashiro et al. [13] showed that patients with type-2 diabetic nephropathy and microalbuminuria had increased activity of urinary MMP-9 when s-creatinine and BUN concentrations were still normal. There is evidence, in my examination of AD fat, of necrosis and hypoxia as well as increased lymphatics and angiogenesis (likely secondary to the hypoxia). Hypoxia can release mediators that cause nerve pain. For fat to grow, many changes occur including activation of enzymes required to help remodel fat tissue called matrix metalloproteinases (MMP)^{14, 15}. The MMPs also function to increase blood vessel growth¹⁶. This is important as there are increased blood vessels in AD as well as in angioliopomas which are found in 30% of individuals with AD¹⁷. To inhibit or decrease fat growth, therefore, an inhibitor of MMPs may be useful.

MMP-1 activity is also highly induced in Alzheimer's disease, and MMP-1 and MMP-3 are involved in the pathophysiology of the disease^{18, 19}. Women with polycystic ovarian syndrome (PCOS) also have elevated levels of MMPs^{20, 21}.

There are many protease inhibitors I know of that are currently available for use. You may need to try one or more before you figure out which ones work best for you:

- 1) A diet rich in **raw grains** – grains are seeds!!!! They must be taken raw not roasted.
- 2) Any **seed extract** such as horse chestnut seed extract (see below), grape seed extract (GSE; which also inhibits atherosclerosis²²) and grapefruit seed extract (no evidence on this yet). Eating raspberries and strawberries so that you consume (and chew) the seeds is also good if you have no contraindications (such as diverticulosis or other).

There are a few manufacturers that seem to have good organic GSE including:

- ❖ <http://www.seagateproducts.com/grape-seed-extract.html> 250mg capsules twice daily
 - ❖ <http://www.opcs.com/> 200mg twice daily (has pure OPCs)
 - ❖ <http://organicpharmacy.org/products/Grape.Seed.Antioxidant/SKU:3252NOW> 60mg 3x daily; 90% OPC
 - ❖ http://www.microtechpro.com/products/prod_opc150antioxidant.htm 150mg twice daily
- ❖ I also like Grapenol 150 mg by Solaray which contains 100% Grape Seed Extract as I prefer to not mix one supplement with many others – it complicates your being able to figure out what works for you and what does not.

❖ If you are tired of taking pills, you can get GSE as a sublingual spray:

<http://store.herbalnutricon.com/sn0489.html>. It comes as a grape-flavored 2 fl oz bottle with a Proanthocyanidolic Value of 95.

A word on horse chestnut seed extract (HCSE; *Aesculus hippocastanum* L.):

There is a ton of research on this supplement including it's anti-obesity properties²³. It has been used for years to relieve varicose veins and *is an MMP inhibitor*²⁴. Aesculaforce is a fresh plant HCSE that is available as an oral tincture, tablets, and as topical gel. HCSE is effective for the treatment of early stage chronic venous insufficiency when compared to placebo. The gel appears to work very well for those of you not wanting to take another pill^{25, 26}.

HCSE Dosage:

- *Tablets/capsules:* 5.0-8.0:1 (w/w): 250.0-312.5 mg extract (corresponding to 50mg aescin) x 2 times a day in delayed release form with a meal^{26, 27}.
- *Tincture:* 20-30 drops (0.5-0.7 ml) x 3 times per day (1:2.6 w/v, 65 vol.-% alcohol) with a meal²⁸
- *Topical gel:* 1g contains 54-177mg dry extract standardized to 2% aescin, applied to area 2 x per day^{26, 28}
- *A few places to purchase pure HCSE:* <http://www.bayho.com/p/826481.html>
- <http://www.smartbomb.com/le00408.html>
- http://www.needs.com/product/Pure_Encapsulations_VeinPro_120/b_Pure_Encapsulations
- AND THE GEL: <http://www.nationalnutrition.ca/detail.aspx?ID=967>

You might also consider combining the GSE and HCSE if you already take GSE and like it. Many stores carry the combination of extracts.

Side Effects

Acute Renal Failure - There have been two case reports of aescin-induced nephrotoxicity²⁹, resulting from high-dose aescin (active ingredient of horse chestnut seed extract) ingestion. There is no change in renal function with 340 mg/kg⁻¹, mild renal impairment with 360 mg/kg and acute renal failure with 510 mg/kg³⁰. In three clinical trials, performed to assess the effect of HCSE on renal failure including in both adults and children, and patients with both normal and impaired renal function, a high therapeutic dose of intravenous whole horse chestnut extract was administered following surgery with no signs of developing or worsening of renal function in any of the patients³¹⁻³³.

Dizziness, headache, pruritis and gastro intestinal symptoms in patients taking oral HCSE are not common (0.9%-3.0%) and are generally mild.

Allergy/Anaphylaxis/Contact Dermatitis - There has been no incidence of allergy or anaphylactic reactions to oral HCSE. One severe case of urticaria and dyspnea has been reported involving a patient in contact with topically applied aescin³⁴. One case report linking 1% aescin proctosedyl ointment with contact dermatitis has been reported³⁵, although negative results were seen in twelve controls using the same dosage. According to the Schweizerisches Toxikologisches Informationszentrum Zurich (1966-1994) there have been 3 case reports of allergy and 3 case reports of anaphylactic shock associated with *Aesculus hippocastanum*.

Hepatic Injury - There has been one case report of drug-induced hepatic injury in a patient who was treated with 65mg intravenous Venoplast® several hours prior to surgery³⁶. Seventeen days after surgery, a liver function test showed mild abnormality and 60 days later, the patient complained of pruritis and jaundice. A moderate of elevation of bilirubin, ALP, gamma-GTP, and eosinophilia were observed.

Delayed Gastric Emptying - In rare cases, the compound aescin Ib isolated from horse chestnut seed may cause irritation in the gastric mucous membranes and may inhibit gastric emptying by the stimulation of capsaicin sensory nerves that in turn releases dopamine followed by a release of prostaglandins^{28, 37}. *If you have delayed gastric emptying you can try a **time-release capsule** taken with a meal.*

- 3) **ACE inhibitors** such as ramipril (↓MMP-2^{38, 39})
- 4) **Omega-3-fatty acids** (↓MMP-1⁴⁰, 2, and -9^{41, 42})
- 5) **L-arginine** decreases inflammation and enhances muscle regeneration⁴³ in part by decreasing the activity of metalloproteinase (MMP)-2 and MMP-9, the two enzymes implicated in retinal ischemia⁴⁴.
- 6) **Pycnogenol** administration decreases MMP-2, MMP-9, and MMP-13 in mice⁴⁵.
- 7) **Antibiotics** such as the tetracycline antibiotics (doxycycline and minocycline). The fluoroquinolones (such as ciprofloxacin) are not recommended for while they inhibit MMP-13, they increase MMP-1, -2, -8 and -9^{46, 47}. The tetracycline antibiotics, primarily doxycycline which is the best studied, seem to help decrease pain and have even caused the lipomatosis to dissolve in some individuals. This may be due to its broad spectrum inhibition of MMPs (↓MMP-1, -2, -3, -8, -9, -10, -13⁴⁸⁻⁵¹). However, they work best when coupled with N-acetyl-cysteine. The dosage of doxycycline is 100mg twice daily and for minocycline is 100 mg three times a week. If fatigue persists, increase the minocycline dosage to daily. I recommend judicious use of this antibiotic (to determine if a breast lump can be reduced, at the time of surgery or a dental procedure, at the time of lithotripsy, or to initially quiet activated MMPs in tissue, whose inhibition could theoretically be maintained by supplements). You must take probiotics with any antibiotic.
- 8) **Lucidenic acids** from the Ganoderma lucidum mushroom (Reishi) suppress matrix metalloproteinase (MMP)-9 activity⁵². Interestingly, NSAIDs may increase the expression of these enzymes at least in the cornea of the eye⁵³.
- 9) **Noni fruit extract** which is in a Phase I Study of Morinda citrifolia (Noni Fruit Extract) in patients with advanced cancer:
(<http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=299070&version=HealthProfessional&pr otocolsearchid=4284850>).

Noni (or nono) juice is from a plant called Morinda citrifolia. Like bananas, noni juice is high in potassium. Traditionally, noni fruit is used to combat fatigue⁵⁴. Although some companies producing this juice suggest a miracle cure for all sorts of diseases which is worrisome⁵⁵, we will focus here on how it may affect the pathophysiology of lipomatosis and potential side effects.

For AD, FML and MSL, we are addressing the remodeling of adipogenesis that must go on to increase adipose tissue. We know this involves MMPs that are present in all tissue and participate in remodeling. In the culture dish (*in vitro*) noni juice, at a concentration of 5%, strongly inhibited the initiation of new vessel sprouts from a model of placental vein explants. At a concentration of 10%, vessel degeneration and apoptosis (death) in established capillary networks were observed. This concentration was effective at inhibiting capillary initiation in explants from human mammary tumors, and led to degeneration of vessels in explants showing capillary sprouting⁵⁶. This means that noni juice may be able to inhibit the formation of blood vessel formation that contributes to lipomatosis. The anthraquinone in noni juice significantly increased elaboration of procollagen type I C-terminal peptide and glycosaminoglycans and reduced expression of the collagenase MMP-1 dose-dependently in human dermal fibroblasts⁴⁰. So in combination, decreased MMP activity and angiogenesis may be beneficial in lipomatosis.

Noni juice also improved wound healing decreasing glucose levels faster in diabetic mice provided

100ml/kg for ten days after wound formation⁵⁷. A quality of life questionnaire (EORTC QLQC30) administered in a phase 1 clinical study of ripe noni fruit extract revealed a dose-dependent improvement in physical functioning and fatigue, where patients felt less weak, needed less rest and were able to participate in more physical activity⁵⁸. A clinical pilot study of Tahitian Noni® Juice (TNJ) in postmenopausal women demonstrated that consuming 120 mL noni juice per day for 3 months improved their global Physical Component Score on the Short Form 36 (SF-36) quality-of-life survey, including the physical function and role-physical subscales that measure ability to participate in vigorous activities, such as running and strenuous sports, as well as moderate activities, such as walking and playing golf⁵⁹. Mice also had longer endurance, balance and flexibility in various trials when fed noni juice⁶⁰.

Side Effects of Noni Juice

There have been cases of hepatotoxicity such as hepatitis reported with the consumption of noni juice⁶¹⁻⁶³. While four patients recovered spontaneously after ceasing intake, the fifth patient underwent liver transplantation. In a recent publication, data from a single-centre, double-blind, placebo-controlled safety study with three dose levels of Noni juice, a daily dose of 750 mL of Tahitian noni juice for 28 days had no measurable effect on clinical parameters of liver function, on blood cell counts and serum chemistry⁶⁴. The anthroquinones from the roots of *Morinda citrifolia* that would have any potential of being hepatotoxic were also not found in the fruit^{65, 66}. Other data suggest that noni juice (fed as 10% extract to mice) is effective in protecting the liver from extrinsic toxin exposure⁶⁷. Obviously, more data is needed and careful examination of noni preparations made. Without an imaging modality for lipomatosis that will allow following lipomatosis in clinical trials, trials of noni juice in lipomatosis are far in the future.

So how much noni juice would I suggest you drink? Postmenopausal women drank 2 ounces of either placebo or noni juice (obtained from Morinda,® Provo, UT) each morning and evening, for 3 months. What you do depends on what you and your doctor are willing to try to improve the lipomatosis. Remember, consumption of anything in excess is not healthy.

10) **Selenium** inhibits MMP-2 but also decreases an inhibitor of MMPs, TIMP-1⁶⁸. I've received one report that selenium decreases weight and pain in one patient with AD. Be aware that selenium may exacerbate glaucoma.

11) **Curcumin with piperine** – Inhibits membrane bound MMP-1 (MT1-MMP)⁶⁹ and is anti-inflammatory by inhibiting MMP-2⁷⁰ and MMP-9⁷¹. It is poorly absorbed so needs to be taken with piperine that inhibits glucuronidation (breakdown) in the intestine⁷² or made lipid soluble. Alternatively, for an oil base Curcumin (turmeric) mask. Get 1 tsp. of Turmeric powder (turmeric powder is available on the grocery store as spice) and 1 tsp. of olive oil or virgin coconut oil. Mix the ingredients until you have a paste like consistency. Apply the mixture on the areas to be treated. For a hydroalcoholic base Curcumin mask. Get 1 tsp. of McCormick Turmeric powder and 1 tsp. of 70% ethanol 30% water rubbing alcohol. Mix the ingredients and then put a small amount over fatty growths. Turmeric powder is available on the grocery store as spice. The topical curcumin powder can be formulated using turmeric powder, water, mineral oil, vitamin-E, glycerin and propylene glycol. You can also buy a CoQ10/Curcumin/D-3 Topical Cream here: http://www.springboard4health.com/store/more_hpl_coq10-cur-d3.html or here: <http://www.healthprolabs.com/product39.html> but it is pricey. Note that the characteristic yellow color of curcumin (turmeric) stains human skin and clothing. The staining effect of curcumin on human skin is very noticeable for persons with light skin complexion. Washing with soap and water may not be

adequate to remove the yellow stain of Curcumin on the skin. It may take several days before the stain disappears.

- 12) "Statin" drugs such as Zocor and Lipitor⁷³ (see below).
- 13) Glucosamine sulfate^{74, 75}.
- 14) Others (see compendium in Table below).

Table of MMP Inhibitors and the MMPs inhibited

Medications	MMP Inhibitor*	MMP(s) Inhibited or Elevated
	Glucocorticoids	↓MMP-1, -2, -7, -8, -9 ^{76, 77} , -13 ⁷⁸
	Androgens	↓MMP-9 ⁷⁹
	Retinoic acids	↓MMP-1, -7 ^{77, 80}
	NSAIDs (Naproxen, meloxicam)	↓MMP-2, -9 ⁷⁶
	ACE inhibitors (ramipril)	↓MMP-2 ^{38, 39}
	Losartan (angiotensin receptor blocker)	↓MMP-8, -13 ⁵⁰
	Clodronate	↓MMP-2, 3, -9, -12 ⁸¹
	Doxycycline (tetracycline)	↓MMP-1, -2, -3, -8, -9, -10, -13 ⁴⁸⁻⁵¹
	ciprofloxacin	↓MMP-13; ↑MMP-1, -2, -8 and -9 ^{46, 47}
Nutraceuticals	Grape seed extract	↓MMP-2 ²²
	Omega-3-fatty acids	↓MMP-1 ⁴⁰ , 2, and -9 ^{41, 42}
	<i>Semecarpus anacardium</i> nut extract	↓MMP-1, -2, -3 ⁸²
	L-arginine	↓MMP-2 and -9 ^{43, 44}
	Pycnogenol	↓MMP-2, -9, and -13 ⁴⁵
	Selenium	↓MMP-2 ⁶⁸
	High-molecular-weight cranberry fraction	↓MMP-3, -9 ⁸³
	Silymarin (family of flavonoids)	↓MMP-9 ⁸⁴

*Not listed are the many synthetic MMP inhibitors in early phase studies.

Side Effects of Synthetic MMP inhibitors: There are a number of clinical trials by drug manufacturers on synthetic MMP inhibitors that have resulted in side effects including edema, palmar fibrosis, Dupuytren contracture, or persistent tendon thickness or nodules, reversible arthralgia, stiffness, and myalgia⁸⁵. This MMP-induced musculoskeletal syndrome in rats included compromised ability to rest on their hind feet, high-stepping gait, reluctance or inability to move, and hind paw swelling⁸⁶. Although these side effects have not been reported for the MMP inhibitors listed above, side effects can occur with any herbal or nutritional supplement. Stopping the supplement should resolve the side effects prompting you to choose an inhibitor for which you do not experience similar problems.

Hypoxia and MMP Inhibitors

Many people with lipomatosis complain of cognitive changes including poor memory. The blood brain barrier (BBB) plays an important role in the homeostatic regulation of the brain microenvironment and maintains the immune-privileged status of the brain by restricting the entry of T lymphocytes. Structurally, the BBB is formed by tight junctions between the endothelial cells. Astrocytes, pericytes and perivascular microglia surround the endothelial cells contributing to proper functioning of the BBB. Hypoxia, associated with disorders such as stroke, cardiac arrest, respiratory distress, carbon monoxide poisoning among many others, disrupts the BBB. Alterations in the endothelial cells such as increased pinocytotic vesicles and derangement of the tight junction proteins may be responsible for increased permeability at the BBB resulting in swelling of astrocyte end feet. The disruption of BBB in hypoxic conditions is multifactorial and may involve factors such as enhanced production of vascular endothelial growth factor (VEGF), nitric oxide (NO) and inflammatory cytokines.

Although future research is needed to look into possible therapeutic strategies to improve the functioning of BBB in hypoxic conditions, experimental studies so far have reported beneficial effect of curcumin, melatonin, simvastatin and minocycline in ameliorating the increased BBB permeability in hypoxic conditions⁸⁷.

Especially in winter, since people with lipomatosis have extra blood vessels that clamp down (close) in the cold to keep the internal body temperature normal, and the tissue becomes hypoxic (oxygen starved). This increases VEGF which causes leaky blood vessels to grow which then increases fat. Please, please everyone get a breathing device to help you improve the strength of your diaphragm and increase the oxygen in your bodies: <http://www.powerbreathe.com/homep.html> or <http://www.heartratemonitorsusa.com/Pages/EXPAND-A-LUNG/expand-a-lung.html>. You can buy a breathing device on the internet but I bet a prescription from your doctor would do the trick (maybe Prosthetics at your hospital carries it or your pharmacy). The beauty of this device is that you can do the breathing exercises while watching television and reading!! This is not a pill with side effects. It is easy and so worth it. I also want everyone to do dry skin brushing. This will improve oxygenation to your skin. It hurts the first time but you will get used to it.

Another way to oxygenate areas over lipomas is to use niacinamide (niacin; this is the same medicine used to lower cholesterol). You can crush up niacinamide tablets into powder or buy niacinamide capsules to get the powder. You can also buy niacinamide powder at a very good price at www.beyond-a-century.com.

Niacin Powder USP-FCC (Price is \$5.50)

NIACIN USP-FCC, powder. Recognized as effective in promoting healthy cholesterol, triglyceride and GH levels. May cause harmless flushing sensation which you can build a relative tolerance to. Helps to increase blood flow and, taken before sexual activity, niacin can speed and/or intensify response.** 100 grams, \$5.50 Code 103.0 See also: [NAD, code 751.0](#)

Then you can mix this powder into 100% aloe vera gel to make your own version of it. You can order online a base cream that pharmacies use to compound topical creams and gels. It's called Vanicream and can be found at www.psico.com. This might work better than aloe vera gel. Since it should be 4% niacinamide, if you have 2 ounces of gel (or base cream), 4% by weight would be about 2.4 grams of niacinamide. One ounce is 28 to 30 grams. So you would add the powder from five 500 mg capsules or crushed up tablets to 2 oz. of the gel or cream to make an approximate 4% niacinamide product.

Recommendation IV: Inhibit blood vessel growth (angiogenesis) in the lipomatosis

The lipomatosis of AD has increased blood vessels suggesting increased blood vessel growth (angiogenesis) in this tissue. To decrease angiogenesis and therefore lipomatosis, you can try both green tea and grape seed skins or resveratrol, both which contain polyphenols that are able to inhibit several key events of the angiogenic process such as proliferation and migration of endothelial cells and vascular smooth muscle cells and the expression of two major proangiogenic factors, vascular endothelial growth factor (VEGF) and matrix metalloproteinase-2⁸⁸. The protease inhibitors may also help decrease angiogenesis (see above)¹⁶. I recommend you eat the grapes rather than supplement but if you don't like grapes, you can read more about resveratrol here <http://www.resveratrolnews.com/> and purchase a supplement however, no human trials are available on supplements at this time.

Other treatments in the literature could be tried topically over an angiolipoma or lipomatosis that has additional cutaneous blood vessels. Shark liver oil (when purified contains 40% or more of squalene), fish liver oil (rich in squalene and polyunsaturated n-3 fatty acids) and arctic birch ashes tested, alone or in combinations, significantly diminished cutaneous angiogenesis induced by tumor cells, and tumor growth⁸⁹. Squalene can also be found in amaranth (about 4% squalene⁹⁰), olives, palm oil and wheat germ oil which are

vegetarian alternatives. Amaranth oil is also high in omega-3-fatty acids⁹¹. It also can lower your blood pressure and bad cholesterol.

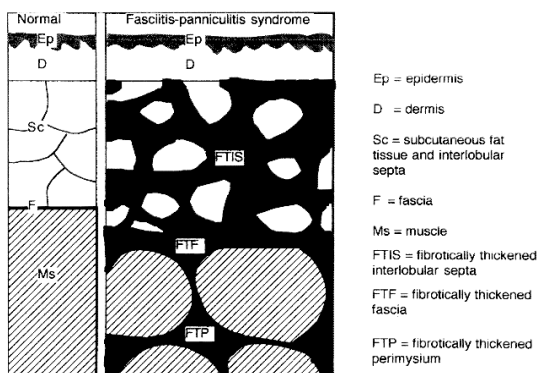
Interestingly, in many people who have AD, they complain of “cherry angiomas” which actually are small telangiectasias under the skin, or dilated blood vessels. In one case report, a 39-year-old woman with a 7-year history of progressive generalized essential telangiectasias who was treated empirically using tetracycline noted a decrease in the telangiectasias within 3 weeks of beginning oral tetracycline, with complete resolution within 3 months. Treatment using tetracycline had been initiated empirically in this patient because of the vascular resemblance to tetracycline-responsive rosacea⁹². The mechanism of action of the amelioration remains obscure but see the section on “Protease Inhibitors” above. Other inhibitors include curcumin, capsaicin, garlic oil, vitamin D3 and glycine (also see glycine in Recommendation V)⁹³.

100% squalene from Daybreak Lavendar Farms is very good at helping diminish telangiectasias:

<http://www.daybreaklavenderfarm.com/store/Only-Facial-Satinizer-100-Olive-derived-span-class-highlight-Squalane-span-pr-16624.html>

Recommendation V: Cimetidine

Although AD is not well understood, the histology of fasciitis panniculitis syndrome (FPS), except for the lipomatosis, is very similar to that of AD^{94, 95}. The skin is not dramatically altered in the FPS but the fascia is increased and can grow into adipose and muscle tissue causing palpable nodules to form (see Figure). Fasciitis



panniculitis syndrome has been successfully treated with cimetidine⁹⁶. It takes 6 months of therapy with cimetidine to see improvement in FPS. Cimetidine (also known as Tagamet) blocks the acid producing cells in the stomach and was initially used in the treatment and prevention of stomach ulcers and can be purchased over the counter.

Cimetidine is currently being used to help in the treatment of breast cancer⁹⁷, brain cancer (glioblastoma)⁹⁸, gastro-intestinal cancer⁹⁹ and colon cancer. It is also used as first-line treatment for warts¹⁰⁰. Cimetidine affects the immune system primarily by

decreasing histamine release by mast cells and basophils where histamine modulates inflammatory and immunological events. The goal when using cimetidine in AD is to modulate the immune system so that it does not attack itself leading to necrosis and pain¹⁰¹ and to inhibit macrophages from recruiting other inflammatory cells into diseased tissue, which cimetidine might do better than corticosteroids¹⁰². In addition, we think that cimetidine will help decrease the vascularity of lipomas causing them to involute; it likely does this by inhibiting a blood vessel growth factor called VEGF¹⁰³. Cimetidine has been shown to modulate the immune system at two doses, 400mg twice daily¹⁰⁴ and 800mg twice daily¹⁰⁵. For people with painful fat, it works well in some, not others. Some individuals found that cimetidine lost its effectiveness after a few months. I recommend taking a holiday from cimetidine whether it works or not then restarting after 7-30 days.

1) This drug must not be started without the knowledge of your physician as it has interactions with many other medications and may increase the amount of those drugs in your blood to toxic levels (see below); 2) Start at 400mg twice daily. If improvements are seen in the lipomatosis, try increasing to 800mg twice daily.

You may add a proton pump inhibitor such as Nexium or other if you experience gastric distress while using cimetidine as cimetidine provides poor relief from gastric reflux and causes it in some individuals.

Are there interactions with other drugs?

Cimetidine is metabolized in the liver where many other drugs are also broken down. There are potential interactions with many other drugs. If you take any of the following, you should check with your physician:

amoxicillin (Augmentin)	fluconazole (Diflucan)
anti-depressants (Elavil)	ketoconazole (Nizoral)
anti-diabetic drugs (Micronase, Glucotrol), metformin (Glucophage)	
aspirin	metoclopramide (Reglan)
benzodiazepine tranquilizers (Valium, Xanax)	metronidazole (Flagyl)
beta-blockers (Inderal, Lopressor)	narcotic (Demerol, morphine)
blood thinners (Coumadin)	nicotine (Nicoderm, Nicorette)
calcium-blockers (Cardizem, Calan, Procardia)	paroxetine (Paxil)
carbamazepine (Tegretol)	pentoxifylline (Trental)
chemotherapy drugs - some	phenytoin (Dilantin)
chlorpromazine (Thorazine)	quinidine (Quinidex, Quinaglute)
cisapride (Propulsid)	sucralfate (Carafate)
clozapine (Clozaril)	theophylline (Theo-Dur)
cyclosporine (Sandimmune, Neoral)	medication for irregular heartbeat (Cordarone, Tonocard, Quindex, Procanbid)
digoxin (Lanoxin)	

If you have chronic kidney disease, chronic liver disease or low sperm count, **using cimetidine might be a problem; check with your doctor:**

Side effects of cimetidine:

Adverse reactions can occur with any drug. Some of these are mild reactions which may go away on their own but if they persist, contact your doctor. For major reactions, contact your doctor immediately.

Minor Side Effects: breast swelling or tenderness in men (gynecomastia), headache, rash, diarrhea, achy joints, dizziness, muscular pain, hair loss, reduced sexual potency, reduced sperm count.

Major Side Effects: hallucinations or mental confusion (more common in the elderly), unusual fatigue, fever, sore throat, shortness of breath, abnormal skin bruising.

Recommendation VI: Oral enzymes

People with AD that do well on cimetidine usually also take oral enzymes by prescription, such as pancreatic enzymes. It is not clear why they work and most traditional physicians like me don't use them much in practice except if one has pancreatic enzyme deficiency. There is, however, some interesting data on an enzyme supplement called serrapeptidase or serratia peptidase (SP). In a number of studies and conditions, SP appears to have anti-inflammatory, anti-edemic and fibrinolytic (breaks up fibrin) activity when taken by mouth. In pill form, SP is destroyed by acid in the stomach and therefore need to be enteric coated where it is passed to the intestine and absorbed¹⁰⁶. SP has been successfully used to treat symptoms associated with chronic airway disease¹⁰⁷, post-operative edema¹⁰⁸ and inflammation after oral procedures^{109, 110} and trauma¹⁰⁸, breast swelling¹¹¹, carpal tunnel syndrome in a small trial in India¹¹², and acute and chronic ear, nose and

throat infections¹¹³. SP has never been used to treat AD in a clinical trial. Side effects include rare pneumonitis¹¹⁴ and blister-like skin eruptions called epidermolysis bullosa¹¹⁵; with any drug or supplement, rare side effects such as these are possible. To avoid other unnecessary side effects from impurities or poor manufacturing, make sure that the supplement is made by an FDA approved GMP certified facility and is marked as 'USP'. I checked out Solaray and Ray Sahelian's brand of products and they are both pharmaceutical grade; you should choose a product that you feel comfortable with.

Recommendation VII: Treat the Lymphatic System

If you have heavy fat or edema in your tissues and you have lipomatosis, you need to drain the lymphatic fluid out of your tissue. This can be accomplished through lymphatic massage and skin brushing. You should be able to find a lymphatic masseuse through your primary physician or ARNP or through the physical therapy department at your hospital. You can also search on the internet at: <http://www.navalta.org/>. For lymphatic brushing, I recommend this site for instruction:

http://www.naturalhealthtechniques.com/healingtechniques/Dry_Brushing_Technique.htm

Recommendation VIII: 'Statin' Drugs

Even if patients with AD do not have 'high' cholesterol, I think it is important to start a 'statin' drug such as pravastatin (Pravachol). If on Tagamet, Pravachol is a good choice as its blood levels are not affected by cimetidine. Other statin drugs such as simvastatin (Zocor) or atorvastatin (Lipitor) or other, are more potent than Pravachol. Statin drugs improve the lipid (cholesterol) profile by decreasing bad (LDL) cholesterol but also serve as an anti-inflammatory drugs to protect vascular endothelium¹¹⁶ and may inhibit collagen production by fibroblasts¹⁰². Statins such as atorvastatin also inhibit MMP-9 in patients having an acute coronary syndrome⁷³! Discuss taking this medication with your doctor as side effects include muscle aches and pain and cimetidine raises statin drug levels.

Recommendation IX: Metformin

People with AD who have impaired fasting glucose or impaired glucose tolerance lose weight on metformin, sometimes in a dramatic fashion; the lipomatosis however, seem unaffected and indeed become more prominent as normal fat is lost next to the growths (lipoatrophy). This loss of fat can be felt as indentations alongside lipomatosis.

Recommendation X: Glycine

In 1938, two investigators described three obese women with AD who had difficulty performing their activities of daily living secondary to fatigue and asthenia (feeling of weakness without actual loss of strength)¹¹⁷. All three women were placed on a diet consisting of 70 grams protein, 70 grams of fat and 100 grams carbohydrate or 1500 calories/day (specifics unavailable). All women were prescribed 10 grams glycine (aminoacetic acid) daily and were able to lose weight but only while taking the glycine. Glycine is a chemically simple and abundant conditionally essential amino acid. It combines with many toxic substances and converts them to harmless forms, which are then excreted. There are glycine binding sites in the central nervous system (CNS). Specifically, the receptor/channel complex, N-methyl-D-aspartate (NMDA), is widespread within the CNS. The NMDA receptor/channel complex consists of an NMDA sensitive glutamate binding site, an associated calcium channel, a glycine binding site, and multiple modulatory sites. If you antagonize the glycine site (prevent glycine from binding or working at the site) feeding in rats increased¹¹⁸. Glycine may therefore be an appetite suppressant. It may also have other effects in the brain promoting weight loss that we don't know about at this time.

One teaspoon of glycine powder provides 2.8 grams of pure glycine if purchased from many different companies including Life Extension and **NOW FOODS**. Glycine powder is inexpensive and easily soluble in juice or water and is not unpleasant tasting. The dose of glycine would be one teaspoon in juice or water three times daily (to reach 10 grams). Glycine may also be anti-inflammatory¹¹⁹. It also blunted increases in intracellular Ca(2+) concentration due to VEGF (it is a VEGF inhibitor)^{120, 121}.

Recommendation XI: Aspirin

Many vessels in AD have fibrin clots when examined by histology. To protect against further damage to blood vessels and fat and muscle tissue, I suggest taking a baby aspirin (81 mg) daily or every other day. If you have lots of bruising or bleeding in the skin, you could take it once a week. Be sure and check with your doctor first.

Recommendation XII: Silver sulfadiazine cream (Silvadene, Flamazine, Thermazine, SSD Cream)

Anecdotal reports from patients with AD suggest that silver sulfadiazine when applied to growths helps with pain. Silver sulfadiazine is known as an antimicrobial and improves inflammation in wounds¹²². Apply a thin film (1/16 inch) of the medication to the affected area and surrounding skin once or twice daily. Propolis cream¹²³ or honey¹²⁴ might work just as well.

Use with caution in: Allergy to any sulphonamide medicine; Decreased kidney function; Decreased liver function; Lack of the enzyme G6PD in the blood (G6PD deficiency)

Not to be used in: Babies less than one month old (neonates); Heavily weeping (exudative) leg or pressure ulcers; Premature infants; Term or near term pregnancy

Side effects

Medicines and their possible side effects can affect individual people in different ways. The following are some of the side effects that are known to be associated with this medicine. Because a side effect is stated here, it does not mean that all people using this medicine will experience that or any side effect. Side effects can include itching (pruritus), a burning sensation, rash, allergy to active ingredients (hypersensitivity) and a decrease in the number of white blood cells in the blood (leucopenia). These side effects may not include all of the side effects reported by the drug's manufacturer. For more information about any other possible risks associated with this medicine, please read the information provided with the medicine or consult your doctor or pharmacist.

Recommendation XIII: Carnitine and CoenzymeQ10

In my recent research both through evaluation of tissue samples or by examining lab results from many individuals with AD, I have been lead to hypothesize that a mitochondrial cytopathy could be exacerbating AD with a defect of beta-oxidation (fat breakdown). In brief, I have found some patients with AD to have elevated lactate and ammonia levels (but not all), low BUN (many – almost all), normal ketones with fasting, and either frankly low or hints of low carnitine (helps break down fat). Some lab recommendations are made below for testing for mitochondrial cytopathy. Unfortunately, at one point in time, if labs are normal, this does not rule out a mitochondrial disorder! In addition, unfortunately, there are no agreed upon standard method of evaluation nor any accepted guidelines to determine whether the diagnosis is correct. However, the labs are a good start in the evaluation. To replace carnitine, I use Carnitor by prescription at 990mg a day in divided doses. The main side effect of carnitine is fish-odor-syndrome. Fish-odor syndrome -- properly known as 'primary trimethylaminuria' -- is caused by excess bodily emission of the compound trimethylamine (TMA).

TMA is a natural byproduct of the digestion of choline-rich foods, such as saltwater fish, eggs, and liver. Reducing the dose of carnitine to 660mg or 330mg a day can alleviate TMA.

With the carnitine I recommend the ubiquinone, coenzymeQ10, 100mg twice daily in an oil/soft gel preparation. Although some data suggest that this supplement does not help mitochondrial disease¹²⁵, other data suggest it might help¹²⁶ and I have anecdotal reports that the oral form and cream form of coenzymeQ10 (CoQ10) help reduce the tumor size and/or firmness in AD. If you want to put it on as a cream, it will be expensive as you need to have it made up with pluronic lecithin organogel as a transdermal delivery system¹²⁷ to get it deep into the subcutaneous fat. There are preliminary reports that CoQ10 in a phospholipid formulation such as this one will decrease blood vessel growth (good if you have angioliipomas) and my hope is that it will also slow down lymph vessel growth which Dr. Dercum described in tissue from a woman with AD over 100 years ago¹²⁸.

Recommendation XIV: N-Acetyl-cysteine (NAC)

NAC is a potent anti-oxidant and has been used in doses up to 1800 mg daily. It reduced hydrogen peroxide in expired air in individuals with chronic obstructive pulmonary disease (COPD) taking 600mg a day for a year¹²⁹ and reduced exacerbations of disease in similar individuals¹³⁰. In another group of individuals with COPD, it was tolerated up to 1200 mg daily and reduced C-reactive protein levels, a marker of inflammation¹³¹. At 1200mg daily, NAC augmented ovulation with clomiphene citrate in women with polycystic ovarian syndrome¹³² and was tolerated up to 1800mg in similar women for 6 weeks¹³³.

NAC is available as an intravenous infusion for inhalation (mucolytic) or as a liquid for treatment of Tylenol overdose.

These are companies that make an oral pill form of USP grade or European GMP grade NAC product:

http://www.bioadvantex.com/us/02_ghealth_pharmanac.asp

http://nybcsecure.org/product_info.php?products_id=202

<http://www.vitaminusa.com/ncy5060ormo.html>

http://healthevangelservices.com/?mainURL=%2Fstore%2Fitem%2Fz3vi%2FSupplements%2FN-Acetyl+Cysteine+60.html%3Fitem_id%3Dz3vi

Take NAC 500-600mg daily.

Cautions: Generally, NAC is well tolerated. However, mild effects such as nausea, headache, tinnitus, urticaria, stomatitis, rhinorrhoea, chills, fever, bronchospasm may be observed. Use with caution if you have asthma. People who are sensitive to sulpha related drugs should not be prescribed NAC. Stop other anti-oxidants when taking NAC.

Cysteine is an amino acid that contains a sulfur dioxide group of atoms in its chemical structure. Upon digestion, some of this sulfur dioxide is released. Not much, but some. For a pill containing 500 mg of cysteine, the amount of sulfur dioxide released is about 30 microgram. You would have to be extremely sensitive to notice such a small amount. If the sulfur in a can of cola (which is about 100-200 micrograms) doesn't bother you, a cysteine pill would be safe too.

Recommendation XV: Lidocaine Patches/Cream/Gel

Intravenous (IV) lidocaine has been used with some success to treat the intractable pain associated with AD¹³⁴⁻¹³⁷. However, the IV lidocaine must be administered under controlled conditions (cardiac monitoring) in a hospital setting and may result in cardiac arrhythmia. Many individuals with AD, however, find relief of pain using lidocaine patches, cream or gel. The lidocaine patches have the highest percent lidocaine.

Recommendation XVI: Labs

There are no lab tests that can be used to diagnose AD. In many cases, all lab tests are normal yet people with AD have complaints consistent with inflammation. However, there are some labs that should be tested prior to treatment and if abnormal, followed throughout treatment. These include:

- 1) ESR – erythrocyte sedimentation rate
- 2) CRP (C-reactive protein)
- 3) SPEP – serum protein electrophoresis
- 4) CBC with differential; eosinophils may be mildly elevated.
- 5) Fasting glucose (many individuals with AD have impaired fasting glucose; high insulin levels and high glucose levels make normal fat grow and therefore most likely, also AD fat).
- 6) Oral glucose tolerance test to evaluate for diabetes (many individuals with AD have impaired glucose tolerance with normal fasting glucose).
- 7) Immunoglobulins including IgM, IgA, IgG and IgE (some individuals have low IgM and others have high IgE or both or neither). High IgE levels should lead to an allergy evaluation.
- 8) Infectious disease work-up: HCV, HIV, ASO, RPR, Lyme disease by western blot, Mycoplasma antibodies. At least 10 different [pathogenic agents](#) have been found to cause obesity in animals. These include [Canine Distemper Virus](#), the RAV7 avian retrovirus and MAM1 avian virus, the [Borna virus](#) in rats (which is also linked to [depression](#) in humans), types of scrapie agent (a [prion](#)), three adenoviruses including Ad-5, Ad-36 (<http://www.obesityvirus.com/page.aspx?page=obetechnresearch>) and Ad-37 which cause fat gain in several species, and [Chlamydia pneumoniae](#) bacteria. Scientists have also found that when mice are infected by general bacteria from the guts of other mice, the recipients' body fat increases.
- 9) Serum total and free carnitine (carnitine shuttles fat to mitochondria in cells to be broken down; if carnitine is low, then losing fat will be more difficult).
- 10) Heavy metal panel to include aluminum.
- 11) IGF-1. May be low in AD.

Recommendation XVII: Pain Management

Pain management should be accomplished between you and your doctor. If your pain is not controlled, my best recommendation would be to see a pain specialist. Many individuals with AD take NSAIDs, antidepressants and use lidocaine patches¹⁷. In the literature, EMLA¹³⁸ and a combination of mexiletine and amitriptyline¹³⁹ have been used to treat pain in AD. Since mexiletine must be administered under a Cardiologist's supervision, many people with AD try amitriptyline for pain taking it one or more times a day and at increased dosage at bedtime.

Recommendation XVIII: Gut Health

Please get evaluated for allergies. Many individuals with AD have allergies and feel better if they are treated and/or avoid allergens including food. If you are unable to see an allergist, try and avoid common food allergens such as milk products, wheat, peanuts or corn, and see how you feel. Take probiotics if you feel you may have dysbiosis (a state of living with intestinal flora that has harmful effects). **Try a fast (such as a juice fast) with a health provider's recommendations if your gut is not improving.**

Recommendation XIX: Surgery (Excision and Liposuction)

Surgery for AD and FML with LD is well-known to relieve pain^{140, 141}. However, it is also well recognized that after major surgery an inflammatory response affects the entire body and its organs and tissues and this is what we are using diet, pharmaceuticals and nutraceuticals to fight against. If you are going to have surgery, double up on your MMP inhibitors and if you can tolerate it, start on doxycycline four days prior to surgery and continue for 1-2 weeks post-surgery (longer if you continue to feel poorly). How long you stay on the doxycycline is up to you and your health care provider.

FOR WOMEN ONLY

Although I have not been able to definitively link flares in AD with the menstrual cycle on questionnaire forms¹⁷, MMPs may play an important role in pre-menstrual syndrome (PMS). For example, tight junctions in the intestine and endothelial (blood vessel) cells change depending on the activity of estrogen through its receptor^{142, 143}. Many alterations in vaginal and endometrial tight junctions are also seen with fluctuations in estrogen. Cells therefore can become leaky as hormone levels change MMP levels. Leaky cells allow for fluid changes and in the gut, may allow for leakage of toxic mediators such as fatty acids. Increased body fat also increases leakiness across gut cells¹⁴⁴. As a woman, you may want to experiment with MMP inhibitors around the time of your menses and see if you can find symptomatic relief from PMS.

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